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Gly Ser Ser Trp Gly Gly Leu Ile His Leu Tyr Thr Ala Thr Ala Arg 35 40 45

Asn Ser Tyr His Leu Gln Ile His Lys Asn Gly His Val Asp Gly Ala 50 55 60

Pro His Gln Thr Ile Tyr Ser Ala Leu Met Ile Arg Ser Glu Asp Ala 65 70 75 80

Gly Phe Val Val Ile Thr Gly Val Met Ser Arg Arg Tyr Leu Cys Met 85 90 95

Asp Phe Arg Gly Asn Ile Phe Gly Ser His Tyr Phe Asp Pro Glu Asn  $100 \hspace{1cm} 105 \hspace{1cm} 110$ 

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Ser Pro Gln Tyr His Phe Leu Val Ser Leu Gly Arg Ala Lys Arg Ala Page 1 Sequence Listing.ST25.txt 130 135 140

Phe Leu Pro Gly Met Asn Pro Pro Pro Tyr Ser Gln Phe Leu Ser Arg 145 150 155 160

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His Thr Arg Ser Ala Glu Asp Asp Ser Glu Arg Asp Pro Leu Asn Val 180 185 190

Leu Lys Pro Arg Ala Arg Met Thr Pro Ala Pro Ala Ser Cys Ser Gln 195 200 205

Glu Leu Pro Ser Ala Glu Asp Asn Ser Pro Met Ala Ser Asp Pro Leu 210 220

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<212> PRT

<213> Homo sapiens

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## Sequence Listing.ST25.txt

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gggggaacgg gcccggaagg ctgccgcccc ttcgccaagt tcatctag	228

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International Bureau





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C12N 15/19

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English

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- (74) Agent: GRUBB, Philipp; Novartis AG, Corporate Intellectual Property, CH-4002 Basel (CH).
- (81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI,

[Continued on next page]

(54) Title: USE OF FIBROBLAST GROWTH FACTOR FRAGMENTS

LTBP2: latent transforming growth factor beta binding protein 2

human vs mouse

hypothetical protein XP\_097406

No match in mouse

ANGPTL1: angiopoletin-like 1

human vs mouse

GPA022 1 CATTELY FORTION CONTROLL STREET LIGHT L

(57) Abstract: A discovery process beginning with an in vivo screening of proteins, peptides, natural products, classical medicinal compound or other substances. The administration of compounds to the animal can be either direct or indirect, such as by the administration and expression of cDNA-containing plasmids. Since the discovery process of the invention is based on a non-preconceived hypothesis and whole organism multi-organ analysis, a compound can be selected for testing in the absence of any biological selection criteria. The resulting organism-wide pattern of the gene expression changes in the transcriptome provides an overview of the activities at the molecular and organism-wide levels. The discovery process of the invention then integrates in vivo profiling and internal and external genomic databases to elucidate the function of unknown proteins, typically within few months. The invention further relates to medical uses of fibroblast growth factor 23 (FGF-23), FGF-23 fragments, FGF-23 C-terminal polypeptides, FGF-23 homologs and/or FGF-23 variants.

WO 2005/045044 A3

## WO 2005/045044 A3

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GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LU, MC, NL, PL, PT, RO, SE,

SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

#### Published:

- with international search report
- (88) Date of publication of the international search report: 10 November 2005

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

Internal Application No PCT/EP2004/012572

PCT/EP2004/012572 A. CLASSIFICATION OF SUBJECT MATTER IPC 7' C12N15/19 According to International Patent Classification (IPC) or to both national classification and IPC Minimum documentation searched (classification system followed by classification symbols) IPC 7 C07K Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched Electronic data base consulted during the International search (name of data base and, where practical, search terms used) EPO-Internal, WPI Data, PAJ, BIOSIS, EMBASE, CHEM ABS Data C. DOCUMENTS CONSIDERED TO BE RELEVANT Citation of document, with indication, where appropriate, of the relevant passages Relevant to claim No. 18-42 X DATABASE Geneseq 'Online! 28 March 2003 (2003-03-28), "Human fibroblast growth factor 23 polypeptide." XP002316719 retrieved from EBI accession no. GSN: ABP58110 Database accession no. ABP58110 the whole document X WO 02/088358 A (GENEPROT INC.) 18 - 427 November 2002 (2002-11-07) the whole document X WO 01/66596 A (CHIRON CORPORATION) 18-42 13 September 2001 (2001-09-13) the whole document Further documents are listed in the continuation of box C. Patent family members are listed in annex. Special categories of cited documents: \*T\* later document published after the International filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the \*A" document defining the general state of the art which is not considered to be of particular relevance invention "E" earlier document but published on or after the international \*X\* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone filing date document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such docu-'O' document referring to an oral disclosure, use, exhibition or ments, such combination being obvious to a person skilled in the art. document published prior to the international filing date but later than the priority date claimed "&" document member of the same patent family Date of the actual completion of the international search Date of mailing of the international search report 08.08.2005 8 February 2005 Name and mailing address of the ISA Authorized officer European Patent Office, P.B. 5818 Patentlaan 2

NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,

Fax: (+31~70) 340-3016

Novak-Giese, S

intermental Application No PCT/EP2004/012572

		2004/012572
Category °	tion) DOCUMENTS CONSIDERED TO BE RELEVANT  Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	JONSSON K.B. ET AL: "Fibroblast growth factor 23 in oncogenic osteomalacia and X-linked hypophosphatemia" THE NEW ENGLAND JOURNAL OF MEDICINE, vol. 348, no. 17, 24 April 2003 (2003-04-24), pages 1656-1663, XP008037462 the whole document	18-42
	i	
		1. 1. 1. 1. 1. 1. 1. 1. 1. 1. 1. 1. 1. 1



Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)
This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:
Claims Nos.:     because they relate to subject matter not required to be searched by this Authority, namely:
2. Claims Nos.: because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).
Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)
This International Searching Authority found multiple inventions in this international application, as follows:
see additional sheet
As all required additional search fees were timely paid by the applicant, this international Search Report covers all searchable claims.
2. As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. As only some of the required additional search fees were timely paid by the applicant, this international Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. No required additional search fees were timely paid by the applicant. Consequently, this international Search Report is restricted to the invention first mentioned in the daims; it is covered by claims Nos.:
18-42
Remark on Protest  The additional search fees were accompanied by the applicant's protest.  No protest accompanied the payment of additional search fees
No protest accompanied the payment of additional search fees.

## FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 18-42

Uses of a polypeptide in the treatment of diseases associated with deregulated angiogenesis, wherein said polypeptide is FGF-23, and variants thereof. Also encompassed are methods for the treatment of above diseases using said polypeptides, respectively pharmaceutical compositions comprising said polypeptides.

2. claims: 1-17

(Business) methods for identifying compounds as a candidate in pharmaceutical development

Internal Application No PCT/EP2004/012572

, Patent document cited in search report		Publication date		Patent family member(s)	Publication date
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